Clinical Techniques in Equine Practice

Update on Topical Wound Medications

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Numerous topical wound medicants are available today. Very few of these products have been tested in the horse. Due to the unique nature of wound healing in the distal limbs of horses (carpus, tarsus and distad), many beneficial effects of these medicants seen in other species and in vitro have not been reproduced in equine limb wounds. There is an abundance of literature regarding topical wound medicants; however, the findings of these studies are quite variable, in general. Many wound care articles have questioned the routine use of topical medications, preferring the concept of moist wound healing in which the body produces all the substrates necessary for adequate wound healing. This article outlines many of the common products that are available to equine practitioners and provides current information regarding their use in wound healing. Unfortunately no product or substrate has been shown to be superior for equine wound management. That being said, the information provided in this article will attempt to provide the practitioner with information necessary to make educated decisions regarding the selection of topical medicants for wound care.

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According to the Business Communication Company, Inc., the estimated market share of topical wound medicants in the human field was 249.1 million dollars in 1990 and it was projected to grow at a rate of 5.9% annually through the year 2005.[1] With this market share available, there are presently numerous new and old products that are marketed for wound care. The difficulty in writing a report on topical wound care products stems from the number of conflicting results in published studies. Additionally, many findings from in vitro tests have not been replicated in vivo. With respect to equine wound management, a favorable outcome documented in other species has not reliably been reproduced when tested in vivo on lower limb wounds of horses. The intent of this report is to provide the practitioner with a review of the currently available topical wound medications and their reported use.

Topical Wound Cleansers and Antiseptics

Wound cleansing solutions should be selected that combine ideal antiseptic properties while minimizing cytotoxicity. These products should be used in the initial phases of wound management to decrease bacterial load and rid the wound of necrotic tissue. Once the wound is clean, physiologic saline solution is ideal for cleansing the wound. Although tap water is acceptable, its hypotonicity will cause cell swelling in which prolonged use can cause significant cell destruction and delay wound healing.[2]

Commercial Wound Cleansers

The cleansing activity of many of the available wound cleansers is dependant on a surfactant that breaks the bonds between foreign bodies and the wound surface.[3] Unfortunately most ionic surfactants and many nonionic surfactants have been shown to be toxic to cells, delay wound healing and inhibit the wounds defenses against infection.[4] A study done to compare some of the available commercial wound cleansers (Constant-Clens, Shur-Clens, Saf-Clens, Cara-Klenz, and Ultra-Klenz) when tested on human fibroblasts, RBCs, and WBCs in vitro concluded that Constant-Clens (Kendall Company) was the most biocompatible.[3] To our knowledge no in vivo studies have been done to prove its efficacy.

Antiseptics

Antiseptics are used early in the wound healing process primarily to reduce bacterial numbers and subsequently to reduce the chances of infection. Antiseptic solutions are contraindicated in clean wounds because they all have some toxic effects that may do more harm than good.[3]

Hydrogen Peroxide (3%)

Hydrogen peroxide is an effective sporocide, but has a narrow antimicrobial spectrum. At a 3% solution, hydrogen per-

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oxide has been shown to be cytotoxic to fibroblasts and result in thrombosis of microvasculature.[5] The cellular toxicity of hydrogen peroxide to fibroblasts exceeds its bacterial potency, therefore it is unsuitable as a wound cleansing solution.[6] Hydrogen peroxide appears to be an effective chemical debriding agent.[3]

Povidone Iodine

Povidone iodine 10% solution has a broad range of antimicrobial activity that lasts for 4 to 6 hours following application. Solutions diluted to 0.1%-0.2% (10-20 mL/1000 mL) are recommended to minimize cytotoxicity and increase the availability of free iodine for its antimicrobial action. At this concentration the solution kills bacteria within 15 seconds and there is no known bacterial resistance to the product. In an ex vivo rat model, 10% povidone iodine ointment (Betadine) was shown to have a negative effect on microcirculation.[7] Povidone iodine is inactivated by organic material and blood. Serum has been documented to inactivate povidone iodine within 2 minutes of contact.[8] Hyperthyroidism, thyrotoxicosis, and hypothyroidism have been reported in people subjected to repeated treatment with and use of povidone iodine.[9-11] Many of these cases are transient and the people return to normal following discontinued use of the compound. When povidone iodine is combined with surfactant to form a detergent it was found to be harmful to wound tissues and potentiate infection.[12] Dermal hypersensitivity is associated with the use of povidone iodine in humans and small animals; however, this reaction is not regularly observed in the horse.

Chlorhexidine Diacetate (2% Solution)

Chlorhexidine has a wide antimicrobial spectrum and prolonged residual effect due to its ability to bind protein in the stratum corneum. Advantages that chlorhexidine has over povidone iodine are its residual antibacterial capacity, continued activity in the presence of blood, pus, and organic debris with less systemic absorption. A potential drawback is that *Proteus* and *Pseudomonas* have developed or have an inherent resistance to this product and it has no effect against fungi or Candida.[13] Contact with the tissues of the cornea must be avoided since ocular toxicity does occur with direct contact. There are multiple studies published evaluating the cytotoxic effects of chlorhexidine. Historically, in vitro cytotoxicity studies have been unreliable as predictors of in vivo wound activity. An in vivo controlled trial using full thickness wounds in dogs irrigated daily using low pressure lavage with various preparations of 0.05% chlohexidine diacetate found no significant difference in the percent of wound contraction, percent epithelialization, or percent healing compared with controls irrigated with either sterile water or LRS titrated to pH 7.4.[14] The only significant difference found in this study was that of in vitro bacterial testing in which all chlorhexidine solutions had 100% kill rate.[14] In another in vivo study involving full thickness wounds in dogs, chlorhexidine (0.05%, 0.5% and 1.0%) solution was found to be superior to povidone iodine solution (0.1%, 0.25%, and 0.5%) in reducing wound tissue bacteria at 48 hrs.[15] When comparing in vivo wound healing in dogs using 0.5% chlorhexidine solution versus 1.0% povidone iodine, the authors concluded that wound irrigation with chlohexidine diacetate (CHD) favored rapid healing and contraction over that seen with povidone-iodine or saline.[16] This study also concluded that cytotoxicity in vitro is not an adequate model for the study of antiseptic effects on wound healing.[16] Currently a 0.05% solution (1:40 dilution = 25 mL of CHD to 975 mL of solution) is recommended for wound lavage.[5]

Dakin's Solution (DS) Sodium Hypochlorite

The use of DS solution was established by Alexis Carrel in World War I for the treatment of open wounds.[17] DS has a broad antimicrobial spectrum. It has been shown to be more effective than povidone iodine and chlohexidine in killing *Staphylococcus aureus*.[18] The bactericidal effect is from the release of chlorine and oxygen. DS has been shown to be cytotoxic to fibroblasts in vitro at concentrations of 0.025% and has a narrow margin of safety.[19,20] The clinical indication for Dakin's solution is to aid in removal of necrotic tissue, thus it should never be used to pack a clean wound.[3] Although DS should not be used routinely as a topical disinfectant, if it is used for debridement it is suggested that it be diluted to one-quarter strength (0.125%).[21]

Topical Antibiotics

Topical antibiotics are most effective when applied within three hours after wounding.[5] However, if the wound is completely debrided, thus creating a new wound, they can be applied within three hours of debridement and are considered effective.

Triple Antibiotic Ointment (Bacitracin, Polymyxin B, and Neomycin) (TA)

TA has a wide antimicrobial spectrum but is ineffective against *Pseudomonas aeruginosa*. [6] The zinc component of bacitracin has been shown to stimulate epithelialization (increasing it by 25%), but can retard wound contraction. These antimicrobials are poorly absorbed, therefore, toxicity is rare.

Silver Sulfadiazine (SS)

SS has a wide antimicrobial spectrum including the *Pseudomonas* spp. and fungi. It has been shown to increase epithelialization by 28% in some studies, and in others it has been shown to slow epithelialization and it may cause increased wound fragility.[22] Muller (2003) reported that using the combination of *Aloe vera* with SS reverses the inhibitory effects observed when using SS alone.[23] Recently, Berry (2003) reported that an increased rate of epithelialization or decreased rate of wound contraction seen in other species, when SS was applied topically, was not observed in horses.[24] The use of a topical slow-release SS product is recommended without a bandage if protection of deep structures, reduction of edema or mechanical stabilization are not necessary.[24]

Nitrofurazone Ointment (NFO)

NFO has a good antimicrobial spectrum against Gram-positive and Gram-negative organisms, but has little effect against *Pseudomonas* spp. It has been shown to decrease epithelialization in laboratory animals and humans by some 24% and it delays wound contraction in horses.[5] It is the antibiotic Furacin that is responsible for the delay in wound healing and not the vehicle base.

Gentamicin Sulfate (GS)

GS has a narrow antimicrobial spectrum but it may be applied to wounds infected with Gram-negative bacteria, par-

ticularly *Pseudomonas aeruginosa*. In a canine study where the rate of wound healing of full surface skin defects was compared when a 0.1% GS solution or a 0.1% oil-in-water cream base was applied topically, they found that treatment with the 0.1% oil-in-water cream base slowed wound contraction and epithelialization.[6]

Cefazolin (C)

C is an effective antimicrobial against Gram-positive and some Gram-negative organisms. When it is applied at 20 mg/kg, it provides a high concentration in the wound fluid above MIC for longer periods than systemically administered C at the same dose. The powder form provides a prolonged tissue concentration compared with the solution. Because of this, C may be effective in treating established infections.

Granulation Tissue Suppressing Agents

Corticosteroids (CS)

CS may be applied topically to suppress the early formation of healthy exuberant granulation tissue, thus facilitating epithelialization and wound contraction.[5] The ability for some CSs to suppress the formation of exuberant granulation tissue in the early phases of healing maybe related to their ability to selectively decrease the release of pro-fibrotic TGF-β1 and β2 from monocytes and macrophages.[25] If CSs are applied after five days in the wound healing process, there appears to be minimal deleterious effect on wound healing.[26] That being said continued application is not recommended since it may also exert negative effects on wound contraction, epithelialization and angiogenesis.[27] Generally the CS is applied at the earliest signs of the formation of exuberant granulation tissue, one or two applications is usually all that is needed to provide the desired effect. CS should not be applied to an infected wound.

Activated macrophage supernatant (AMS)

Although some studies indicate that AMS may improve wound healing in horses and ponies because of its inhibition in vitro of equine fibroblast proliferation, no significant in vivo effects were found in one equine study.[28]

Topical Herbal Therapies

Herbal preparations are only one component of alternative medicine, which encompasses a wide variety of approaches. A large number of herbal therapies and combinations of therapies presently exist for wound care. In general, these preparations are comprised of small amounts of the plant combined into a delivery substance (eg, ointment). The authors have attempted to comprise a list of those herbs readily available from the scientific literature, the source from which the herb is obtained is contained in parenthesis. However, due to the under-representation of herbal therapies in scientific literature, this list is undoubtedly incomplete. Very few of these therapies have been tested scientifically in the horse for effectiveness and/or toxicity. The authors highly recommend further study by those interested in using herbal remedies. See Table 1 for an outline of herbal products marketed in veterinary medicine.

Aloe vera (AV)

AV is reported to stimulate wound healing, have antibacterial, antifungal and antiviral properties, act as an immune stimulant, have antiinflammatory effects and stimulate collagen production.[29] AV extract gel with acemannan has been shown experimentally to increase epithelialization and wound healing in open pad wounds in dogs at seven days.[6]

In a controlled clinical trial, done in women, where wounds were allowed to heal by second intention, the AV gel-treated group had a significant delay in wound healing.[30] Aloe vera is reported to be effective against *Pseudomonas aeruginosa*.[31] Investigators have demonstrated the antiinflammatory effect of AV gel in vitro when tested on human colorectal mucosa in vitro. Their results show reduced production of reactive oxygen metabolites and prostaglandin E2, but failed to show an effect on thromboxane B2 production.[32] In an in vivo rat burn model, AV significantly reduced the amount of leukocyte adhesion, TNF-alpha, and IL-6 at the wound site.[33] Its efficacy in horses has not yet been investigated.

Comfrey (*Symphytum officinale*) (C)

C historically has been used as a natural poultice that reportedly draws exudate and waste products away from the wound.[34] Although, scientific literature is lacking to support or refute this claim, there is evidence that C does have antimicrobial and antifungal properties. Staphylococcal, streptococcal, yeast, coliform, pseudomonas, and some fungal organisms have been killed in as little as 10 to 30 minutes with comfrey extract.[35] Karavaev (2001) demonstrated a strong antifungal activity when comfrey was applied to wheat seedlings.[36]

Eucalyptus (*Eucalyptus* spp.) (EU)

Antibacterial properties of EU against Pseudomonas aeruginosa have been reported in human burn patients.[37] There are also a few reports in the veterinary literature that support the use of EU in wound care.[38-40] Most products tested in these reports contained numerous ingredients and the trial control/design were questionable. Perhaps the best use of eucalyptus in wound care is to treat and/prevent myiasis.[41]

Goldenseal (*Hydrastis canadensis*) (GS)

To the author's knowledge there are no scientific reports currently available that address the use of GS for wound healing. GS has been used for treatment of athlete's foot and minor skin abrasions in people. Antibacterial properties associated with the constituents of GS have been reported.[42]

Jojoba Oil (*Jojoba* spp.) (JO)

To the author's knowledge there are no scientific reports currently available that address the use of JO for wound healing. Historically, JO has been used as a hair conditioner and skin lubricant. Currently it is used as an ingredient in shampoos, moisturizers, sun-screens, hair conditioners, and as industrial machine lubricant. Recent literature has documented JO as a potential sensitizer causing allergic reactions in people such as erythema, vesicle formation and puritis.[43,44]

Propolis (Honey Bee) (P)

P is a compound used by bees to protect there hives from bacterial and viral infections. P is made up of resinous compounds and balsams (55%), beeswax (30%), aromatic oils

Table 1 Topical Products with Reported Wound-Healing Properties

Product	Ingredients	Contact Information
Bag Balm	Petrolatum, lanolin, 8-Hydroxyquinoline sulfate	Dairy Association Co, Inc. PO Box 145 Lyndonville, VT 05851 Phone 800-232-3610 Fax 802-626-3433 www.bagbalm.com
Derm-Assist	Thymol, camphor, propylparaben	Vissil International 935 8th Street Baraboo, WI 53913 Phone 800-472-5464 www.vissil.com
Espree 3 in 1 Wound Cream	Aloe vera, yeast extract, herbs, eucalyptus, bitrix	Espree Animal Products, Inc. 637 Westport Parkway #208 Grapevine, TX 76051
Pavia Natural Wound Care Cream	Lanolin, bees wax, propylene glycol, DI water, vegetable oil, propolis tincture, comfrey extract	Pavia Sales Group, Inc. 1713 Yorkshire Ave. S Minnetonka, MN 55305 Phone: 952-593-0790 Fax: 952-593-9544
T-ZoN Dermal Care Cream	Tea tree oil, hydrocortisone, aloe vera, ethyl oleate, lignoceryl erucate, benzathonium chloride	Healing Tree Products Inc. Eric Witherspoon, DVM McMinnville, OR 97128 Phone 800-421-6223 www.healing-tree.com
Tea-Clenz Anti-Microbial Concentrate®	Benzathonium chloride, tea tree oil	Healing Tree Products Inc. Eric Witherspoon, DVM McMinnville, OR 97128 Phone 800-421-6223 www.healing-tree.com
Tea-Pro Wound Spray	Tea tree oil, comfrey, myrrh, aloe vera, goldenseal	Healing Tree Products Inc. Eric Witherspoon, DVM McMinnville, OR 97128 Phone 800-421-6223 www.healing-tree.com

(10%), and bee pollen (5%).[45] P also contains various flavenoids, amino acids, B vitamins, and antibiotic substances.[45] When applied topically, P has been shown to have a significant antimicrobial activity against Gram-positive bacteria and yeasts, but not against Gram-negative bacteria.[46] A synergistic effect of P extract and antibiotics against *Staphylococcus aureus* has been identified.[47] A marked synergistic effect was demonstrated with streptomycin and moderate effects with penicillin G, doxycycline, cloxacillin, chloramphenicol, cefradine, and polymixin B.[47] Ampicillin failed to produce a similar synergistic effect in this study.[47]

P also has been shown to have antiinflammatory properties. In a cisplatin-induced nephrotoxicity rat model, P demonstrated a free-oxygen radical scavenging ability.[48] It is hypothesized that P's antioxidative capacity comes from its ability to donate a hydrogen atom in vitro[49] and/or the activity of the flavenoids.[50]

Tea Tree Oil (*Melaleuca alternifolia*) (TTO)

TTO products anecdotally are nonirritating, increase fibroplasia without causing the formation of exuberant granulation tissue, provide rapid healing, and are capable of controlling bacterial/fungal infections.[34] TTO's antifungal and antibacterial characteristics of TTO have been well documented.[51-53] To the author's knowledge there is no scientific literature that documents the effects of TTO on wound healing in horses. Takarada (2004) reported that at a concentration of 0.2% TTO had little effect on cultured human umbilical vein endothelial cells.[53]

Thymol (*Thymus* spp.) (T)

To the author's knowledge there are no scientific reports currently available that address the use of T for wound healing. One in vitro study reported a potent antifungal effect against *Candida* spp when the essential oils of *Thymus* were used.[54] Thymol has shown strong antimicrobial activity in vitro against *Staphylococcus aureus* and *S. epidermidis* independent of drug susceptibility patterns.[55]

Enzymes for Wound Debridement

The horse has a propensity to produce excessive granulation tissue, particularly on the lower extremities.[56,57] Various substances have been tested to treat or prevent exuberant granulation tissue. At this time, it is uncertain whether or not enzymes are beneficial and if they have a place in veterinary medicine. A review of the more commonly used enzymes and potential uses are described below.

Trypsin (TR)

Human burn wounds were examined for the presence of TR-like enzymes in the wound during the healing process. The study patients were severely burned children under 16 years of age. Dressings that are dissolved by TR and collagenase were placed on the surgically debrided wounds or on naturally occurring granulation tissue 11 to 48 days post burn. The proteolytic activity occurring in the burn wound digested the dressings.[58] This suggested that enzymes are a natural part of host defenses in the wound healing process and, possibly, that application of enzymes could potentially aid in the wound healing process. This study also concluded that wound enzyme activity and bacterial contamination are not related.[58]

It is hypothesized that TR has antiinflammatory action. Application of one milligram of TR to the wound before application of topical antibiotic was ineffective in potentiating antibiotic activity.[59] Debriding preparations presently available must be used with caution as bacteremia has been reported in human patients following enzyme debridement.[60]

Elase (E)

E, or fibrinolysin-deoxyribonuclease, has been used in everything from treatment of monilial vulvovaginitis to chronic leg ulcers and burn wounds. E has been examined as a possible enzymatic agent to aid in antimicrobial treatment of contaminated wounds. Topical application of the active enzymes in E to contaminated wounds before antibiotic treatment did not alter the incidence of infection.[59]

E powder has been evaluated in patients with chronic leg ulcers before autologous skin grafts. E had a significant effect on debridement and enhancing granulation tissue formation than saline controls.[61] The use of E has been reported to facilitate and extend the necrotic process, in such cases its use has been highly contraindicated.[62]

Granulex (G)

Granulex is an aerosolized spray that contains trypsin (TR), Peru balsam and castor oil.[63] TR functions to debride necrotic tissue from ulcerated areas without harming healthy tissue.[64] Peru balsam contains cinnamic and benzoic acids, believed to act as irritants, resulting in enhanced blood flow by local stimulation of the capillary bed.[63] It may also act as a mild antiseptic.[63] Castor oil is a local protective agent that may promote epithelialization.[63] In one case report, Granulex was used to promote tissue healing of a necrotic ulcer of the oral mucosa. After 48 hours of Granulex spray treatments, the area had granulated and the site of the eschar had become more normalized.[65] A prospective clinical trial in human patients with decubitus ulcers treated with Granulex revealed a faster healing rate than the control group; however this data were not analyzed for statistical differences.[66] Aspiration of Granulex spray is an important consideration if it is sprayed on or around the face as it is oil-based and may cause respiratory irritation.[65]

Meat Tenderizers (MT)

Users of MT, anecdotally profess it to have a debridement activity when applied to open wounds. The response seen has been variable among practitioners and individual cases. This variability in response is most likely a result in the varying concentrations and differing enzymes present in different products. Scientific studies regarding the use of these products in wound care is lacking. Most literature focuses on MT's use for providing analgesia following jellyfish stings. In all cases MT was found to be ineffective as an analgesic.[67]

Maggot therapy (MT)

Biosurgery has recently experienced a renewed interest in human medicine for wound management because of the recognition of the many antimicrobial resistant bacteria spp that have been identified.[68] Maggots are believed to work by producing potent proteolytic enzymes that digest necrotic tissue. To our knowledge its use in equine wounds has not been investigated.

Other Topical Agents

Live Yeast Cell Derivative (LYCD)

LYCD is a water soluble extract of yeast reported to stimulate angiogenesis, epithelialization, and collagen formation.[14] It has been associated with improved wound healing in dogs. However, in horses, it prolonged wound healing by delaying wound contraction and resulted in excessive granulation tissue formation.[69]

Honey (H)

H has many potentially useful properties including; a broad spectrum antimicrobial activity, antiinflammatory actions and stimulation of new tissue growth.[70] Although the exact mechanisms of H's bacterial inhibition is unknown, possible mechanisms include; an osmotic action, low pH, its viscous nature and production of hydrogen peroxide.[71] H's antimicrobial effects have been demonstrated in vitro against 18 strains of methicillin-resistant *Staphylococcus aureus*, 7 strains of vancomycin-sensitive enterococci and 20 strains of vancomycin-resistant enterococci.[72] This latter study concluded that inhibition of bacteria was not solely dependent on osmolality.[72] Bang and coworkers (2003), described the antibacterial effect of H as a result of hydrogen peroxide production by glucose oxidase in the wound.[73] The concentrations of hydrogen peroxide produced in this study were very low, therefore cytotoxicity is considered to be very low. Further studies have shown that H contains inhibine, an enzyme from bee pharyngeal glands, which breaks down to hydrogen peroxide and glucolactone/gluconic acid; these act as a mild disinfectant and mild antibiotic, respectively. Honey also provides antioxidants which protect wound tissues from the damage imparted by free oxygen radicals released from inflammatory cells.[74] Finally, H treated wounds had little neutrophilic infiltration but show a chemo-attractant effect for tissue macrophages and marked proliferation of angioblasts and fibroblasts.[19] H has been shown to enhance granulation tissue formation and epithelialization, possibly via their stimulatory activity on the tissue macrophage.[75] In particular, it has recently been shown that the stimulatory effect of honey on wound healing may in part be related to the up-regulation of inflammatory cytokines (TNF-α, IL-1β, IL-6) within monocytes.[76] Sources of H from Australia and New Zealand (*Leptospermum* spp.) have been identified as having enhanced antimicrobial activity.[77] Natural manuka and pasture H have superior antimicrobial activity when compared with artificial H.[72]

Kingsley (2001), concluded from a series of case studies that not all the expected beneficial effects of using honey for wound treatment are realized in clinical practice.[70] A review of randomized controlled trials involving H in superficial burns and wounds concluded that the quality of these studies were low, and confidence in honey as a useful treatment for superficial wounds and burns was low although there appears to be a biological plausibility of its use.[78]

Lanolin (L)

L has been used for centuries as a skin softener and moisturizer. In a controlled clinical trial evaluating partial thickness wounds in piglets, it was found that lanolin cream alone significantly enhanced the rate of epithelialization and increased dermal thickness when compared with lanolin–human epidermal growth factor cream or gauze controls.[79] Lactating women reportedly had significantly more pain when using L dressings versus a hydrogel dressing.[80]

Phenytoin (PT)

PT was introduced in 1937 as an antiseizure medication, since that time there has been interest in its use as an adjunct to wound care.[81] Intramuscular and topical PT treatment for wounds has been shown to shorten healing time in a rabbit model evaluating superficial and deep wounds.[82] This study also found that topical use of PT resulted in better wound tensile strength when compared with systemic treatment. In a controlled human clinical trial, PT treated skin ulcers healed in 73% of cases compared with saline dressed (control) skin ulcers at 28.5%.[81]

Galium Nitrate (GN)

GN acts in wounds by increasing expression of type I collagen and fibronectin in human fibroblasts, which are structural components of the wound matrix.[83] GN also suppresses matrix metalloproteinase (MMP) activity and accelerates in vitro keratinocyte motility.[83] Too our knowledge no information is available regarding GN′s efficacy when used clinically.

Gentian Violet (GV)

GV is often applied topically in a 1% aqueous solution. It has been proposed to be an effective wound repair stimulant, though conclusive evidence is yet to be established. There are several potential side effects that must be considered before it is determined whether or not this agent should even be used. In one study, three human patients developed a necrotic, painful and slowly healing skin reaction after application of 1% GV in aqueous solution.[84] GV is also noted to have a tissue-irritating effect that discolors and masks the true color of the skin, necessitating caution when using this agent in an ulcer.[85]

GV in low concentrations inhibits the formation of granulation tissue in cellulose sponges implanted subcutaneously for 10 days in rats.[85] One application of GV to incisional skin wounds before suturing retarded the development of strength in the wounds for greater than three weeks.[85] It also caused marked vascular proliferation, indicating tissue damage as assessed by microangiography.[85] Finally, granulation tissue slices exposed to GV have a decreased capacity to consume oxygen, to incorporate 14-C proline into collagen and noncollagenous proteins, and to synthesize RNA.[85] Several studies have revealed that GV is a carcinogenic agent when used on open wounds and on mucous membranes.[86,87] GV is not recommended for wound care.

Recombinant Vasoactive Protein (RVP)

RVP is a recombinant protein originally found in insect saliva. This compound has recently been evaluated for wound healing because it is known to increase blood flow. In a controlled clinical trial using surgical wounds in dogs it was found that intradermal or subcutaneous injection of RVP significantly increased wound breaking strength on day 5.[88] The rate of open wound healing was significantly enhanced at day 21 in dogs treated with RVP intradermally at time 0.[88]

Scarlet Oil (SO)

SO has been used in the wounds of horses for many years. There have been no controlled studies published that evaluate its use in equine wounds. The ingredients are: mineral oil, isopropyl alcohol (30%), methyl salicylate, benzyl alcohol (3%), pine oil, eucalyptus oil, parachlorometaxylenol, and biebrich scarlet red.[89] Pine oil is used commonly as an antiseptic in household cleaning agents. The use of eucalyptus (EU) has been described previously in this report. The use of SO can cause a painful contact dermatitis in some horses making continuation of treatment challenging. Most veterinarians use this agent to stimulate granulation tissue formation in large upper body wounds. There is no data to prove that it is of any benefit.

Aminoplex (AP)

AP contains amino acids, trace minerals, peptides, electrolytes, and nucleosides. The purported properties of AP include; the ability to reverse cell damage, increase glucose + oxygen uptake, enhance collagen synthesis, and accelerate epithelialization.[90] In a controlled human clinical trial using AP following CO_2 laser resurfacing, patients that received AP therapy had decreased postoperative pain, healed faster, and had less swelling than that observed in a more traditional laser recovery program.[91]

No data are available documenting its use in the horse.

Sugardine (SD)

SD is made by adding povidone iodine solution to granular sugar until a workable paste consistency is reached. This hypertonic agent acts by osmotic action to draw exudate from the wound. When using SD be aware of the information included under povidone iodine in this report. For more information on the use of hypertonic wound products the reader is referred to Ted Stashak's article, "Update on Wound Dressings," in this publication. This agent is commonly used on the foot to treat a subsolar abcess.

Zn7 Equine Wound Care Formula (ZE)

ZE is produced by Addison Biological Laboratory, Inc. It is a wound cream comprised of deionized water, zinc gluconate, carboxymethylcellulose, taurine, L-lysine, methylparaben, and propylparaben.[92] According to the company, product provides substantial antipruritic, antimicrobial, and wound healing benefits. The majority of the literature surrounding zinc gluconate is associated with its use in lozenges to treat the common cold in people.[93] Zinc gluconate has been shown, in vitro, to stimulate a select group of integrins that affect cellular mobility in the early phases of wound healing.[94]

Controversy exists as to whether zinc aids in wound healing; however, it is well known that zinc deficient animals have impaired healing which is reversed with appropriate supplementation.[95] When zinc oxide was examined on full-thickness wounds in pigs, researchers found that IGF-1 mRNA was significantly increased on days 3 to 4 postwounding.[96] This finding could be a mechanism by which zinc may enhance wound healing. Zinc oxide was also found to significantly increase re-epithelialization of partial-thickness skin wounds in pigs when compared with treatment with zinc sulfate, which indicates that the mode of delivery is probably critical to achieve the beneficial effects of zinc.[97] No data are available documenting its use in the horse.

Tripeptide–Copper Complex (TCC)

TCC is available (Lamin ProCyte, Corp, Kirkland, WA) as a topical or injectable medicant. Reportedly the product promotes neovascularization, epithelialization, collagen deposition and enhances wound contraction.[98] The topical form has been shown to enhance open wound healing in dogs and the injectable form stimulates type I collagen deposition in healing pad wound in dogs. TCC has also been shown to enhance healing of chronic ischemic wound. To our knowledge TCC is not commonly used in equine practice at the time of this writing.

Vitamin E (E)

E is the major lipid-soluble antioxidant in the skin, however its effects on surgical wounds is inconclusive.[99] Parenteral supplementation of vitamin E in rats has been shown to significantly increase epithelial thickness, fibroblast proliferation, and neovascularization in rat tympanic membrane perforations.[100] In a double-blinded clinical trial to evaluate the effects of vitamin E on the cosmetic appearance of scars in people, it was found that vitamin E had no effect and it resulted to a high incidence of contact dermatitis.[101]

The use of Intracell, ACE Mannan, Iodosord, Soloseryl, Solugel, Tripeptide-copper, TGF-B, Sugar, and Elk Velvet is addressed in the article "Problems and Proposed Innovative Solutions," by C. Theroet in this publication.

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